"Emerging" Pollutants, and Communicating the Science of Environmental Chemistry and Mass Spectrometry
– Pharmaceuticals in the Environment –

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While this paper is to a large degree targeted for those not familiar with mass spectrometry[†] – a primary focus is on the importance of mass spectrometry in ultimately protecting public health and minimizing risks of chemical exposure. Its other audience is those who practice in this specialized field. Lest this subject not interest you, by reading this article one can discover among other things:

Why elevator rides can be important for your career and for your discipline.
Why acetaminophen is used for brown tree snakes – or lipid-lowering drugs for pigeons.

[†][for an overview of mass spectrometry, a number of excellent web sites are available, including those at: http://base-peak.wiley.com/links/Resources/Educational_Resources/]

This paper weaves a multi-dimensioned perspective of mass spectrometry as a career against the backdrop of mass spectrometry's key role in the past and future of environmental chemistry. Along the way, some insights are offered for better focusing the spotlight on the discipline of mass spectrometry.

A Foundation for Environmental Science – Mass Spectrometry: Historically fundamental to our understanding of environmental processes and chemical pollution is mass spectrometry. This branch of analytical chemistry is the workhorse that supplies much of the definitive data to environmental scientists and engineers for identifying the molecular compositions, and ultimately the structures, of chemicals. This is not to ignore the complementary and critical roles played by the adjunct practices of sample enrichment (e.g., to lower method detection limits via any of various means of selective extraction) and analyte separation (e.g., to lessen contaminant interferences via the myriad forms of chromatography and electrophoresis).

While the power of mass spectrometry has long been highly visible to the practicing environmental chemist, it borders on continued obscurity to the lay public and most non-chemists. Even though mass spectrometry has played a long, historic (and largely invisible) role in establishing or undergirding our existing knowledge about environmental processes and pollution, what recognition it does enjoy is usually relegated to that of a tool. It is usually the relevance or significance of the knowledge acquired from the

application of the tool that has ultimate meaning to the public and science at large – not *how* the knowledge was acquired.

Communicating Science – Mass Spectrometry and the "Risk Paradigm": Protecting human and ecological health from chemical hazards is rooted in assessing and managing/controlling chemical risks – a process requiring data from many aspects of the "risk paradigm". Comprising this "paradigm" are a series of inter-related steps or activities, such as identifying sources, establishing environmental occurrence, elucidating fate and transport, verifying exposure or effects (e.g., bio-markers), and developing remediation/control technologies. Mass spectrometry plays a critical, direct role in all of them, except the actual step of assessing risk (Fig. 1). Mass spectrometry is essential to obtaining data required for establishing: environmental source/origin, occurrence (identities and concentrations), fate and transport (including that for all associated transformation products), exposure (including measurement of biomarkers), effects (including receptor interactions and metabolites), and finally, measuring the effectiveness of mitigation, remediation, and engineered treatment measures and technologies.

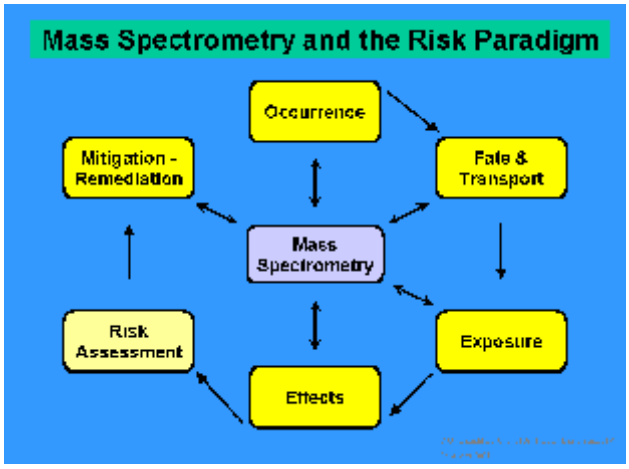

Figure 1. Central role of mass spectrometry in elucidating the risks associated with environmental pollutants.

Often absent in the practicing scientist's time-consuming quest to advance our understanding of the chemical world is a concerted effort to explain to scientists who do not rely on mass spectrometry and to the lay public the importance of the tool – its unique abilities and what it can do. An imperative in the continued health of a scientific discipline is the "marketing" of its worth and ensuring that it has a measurable impact or ***outcome*** – one valued by society. Historically, the value of environmental chemistry has focused on establishing a fundamental understanding of long-existing environmental issues and principles – pollutant identification, fate and transport, exposure, many others. A re-focus on elucidating "emerging" issues (proactive vs. reactive science) can improve the visibility of mass spectrometry. This paper discusses the ever-topical subject of "communicating science", in part by using as an example the recent, still-developing topic of **pharmaceuticals as environmental contaminants.**

While mass spectrometry is an immensely powerful tool, like many sophisticated analytical techniques, its numerous incarnations can bewilder the non-specialist. In the final analysis, whether a researcher is extending the capabilities of mass spectrometry as an analytical tool for others to use, or whether it is being used as part of the analytical arsenal to solve chemical mysteries, it is imperative to keep in mind that it is merely a TOOL -- and in general tools rarely interest the public or garner accolades outside their disciplines of incubation and birth. Rather, it is the OUTCOMES from the applications of tools that capture the public's eye. This is the main impetus behind the federal government's implementation of a planning system (The Government Performance and Results Act of 1993 – GPRA) that provides the mandate to Federal agencies to account for program results through the integration of strategic planning, budgeting, and performance measurement, with an emphasis on *outcomes* (e.g., impacts) – as opposed to *outputs* (e.g., publications, patents, citations) [for a perspective on GPRA with respect to science, see:

http://www.nsf.gov/sbe/srs/ostp/assess/nstcafsf.htm/, http://www.nsf.gov/od/gpra/] (Fig. 2). While GPRA's origins derive from the private sector's continued emphasis on performance improvement over the last decade or so, its implementation can be emulated by the science community at large.

If we accept that one of the ultimate missions of environmental science as that of educating the public at large, then it is incumbent on us all to strive to communicate the significance of our work – its impact, relevance, or outcome – in a way that connects with the lay public and which deepens and enriches the perspective with which they view the world. While this ability has rarely ever been a strong aspect in the training of scientists, we can each reach out in our own way to increase the overall knowledge of the public. With an increased public understanding of the complexities of the biophysicochemical interactions of chemicals, humans, and macro- and micro-biota, the public can eventually gain a heightened appreciation for the reality of the uncertainties scientists continually face in developing definitive conclusions and the importance of the analytical repertoire of the analytical chemist – especially the central role of mass spectrometry. Absent a larger understanding and active communication of outcomes and impacts, our work simply ends with an undefined, hanging ellipsis…

If one accepts that an important objective of environmental science is to sharpen society's focus on "personal responsibility and accountability" for the consequences of our actions, activities, and behaviors, then mass spectrometry plays an immensely important (but necessarily low-profile) role. It is hoped that this greater public awareness of environmental issues would lead to better control over the fate of our environment and health.

The canyon separating the general public's knowledge of science from reality is often highlighted and debated. Responsibility for this chasm is relegated to various parties. A telling national survey of general science knowledge was completed in March 2001. The survey was conducted by the California Academy of Sciences and Harris Interactive Polling (http://www.calacademy.org/geninfo/newsroom/releases/survey_results.htm). The results of three questions were particularly illuminating: (1) 53% of adults did not know that the Earth revolves around Sun, (2) 48% had no sense of the percentage of Earth's surface covered by water, and (3) 42% did not know whether humans co-existed with dinosaurs. These results highlight a profound national knowledge gap at a time when a democratic discussion of many, complex technical issues is critical for our future. Meaningful public consensus and informed decisions can only result from a sufficient and widely held knowledge base. Furthermore, the poll indicated that the public most trusts (65%) scientists (not educators) to convey needed information about the natural world; the public (95%) also is extremely interested in learning about the environment. Clearly a responsibility rests with scientists to better communicate the meaning, significance, and impact of their work – in clearly articulated terms.

An Example – "PPCPs": One of the critical roles historically played by mass spectrometry is elucidating the identities of previously unknown or unrecognized ("mystery") pollutants – often referred to as "emerging" pollutants; such "detective" work is sometimes called "environmental forensics". This paper focuses on the still-developing outcome of one such application of mass spectrometry – the elucidation of the widespread environmental occurrence of low-levels of numerous chemical members from the many classes of pharmaceuticals and personal care products (PPCPs), many of which are highly bioactive. The role of mass spectrometry in this emerging issue is clearly evident in the published studies that have identified PPCPs in a range of environmental samples (see studies captured in a comprehensive review [1]).

PPCPs are a diverse group of chemicals, used internally or externally with the bodies of humans and domestic animals (and plants), comprising all drugs (available by prescription or over-the-counter;

including the new genre of "biologics"), diagnostic agents (e.g., X-ray contrast media), "nutraceuticals" (bioactive food supplements such as huperzine A), and other consumer chemicals, such as fragrances (e.g., synthetic musks) and sun-screen agents (e.g., methylbenzylidene camphor); also included are "excipients" (so-called "inert" ingredients used in PPCP manufacturing and formulation). Many PPCPs are highly bioactive, most are polar, many are optically active, and all (when present in the environment) occur usually at no more than trace concentrations. The confluence of these factors presents a number of additional analytical challenges.

While the release to the environment of PPCPs from manufacturing processes is controlled by regulatory means (in the U.S., but not in all countries)[2], PPCPs largely owe their origins in the environment to their worldwide, universal, frequent, and highly dispersed but aggregate and cumulative usage by multitudes of individuals (and by agriculture); continuing and escalating introduction to the marketplace of new arrays of drugs with new modes of action is expected to be fueled by advances in genomics and proteomics. Occurrence of PPCPs in the environment mirrors the intimate, inseparable, and immediate connection between the actions and activities of individuals and their environment.

In addition to the more widely publicized occurrence of antimicrobials and steroidal hormones, over 50 individual PPCPs or metabolites (from more than 10 broad classes of therapeutic agents or personal care products) had been identified (as of 1999 [1]) in environmental samples -- mainly in sewage, surface, and ground waters, and much less frequently in drinking waters. It is important to note that although a number of representatives from small subsets of therapeutic classes have been identified in the environment, numerous members of most classes have yet to be searched for. Many of these "unreported" drugs are among the most widely prescribed medications in the U.S., and little data exists to lead to a conclusion that they do *not* occur. In addition to the table of PPCPs with documented environmental occurrence provided in [1], a complementary list of those that have no occurrence data is provided in [3]. This latter list can serve as a guide for those scientists who are interested in expanding the existing environmental occurrence database.

Portions of the parent form of most ingested drugs are excreted in varying amounts (sometimes in undissolved states because of absorption/metabolic protection by excipients) primarily via the feces and urine. Other portions sometimes yield metabolites possessing bioactivity. Still other portions are excreted as conjugates. Free excreted drugs and derivatives can escape degradation in municipal sewage treatment facilities (removal efficiency is a function of the drug's structure and treatment technology employed); the conjugates can be hydrolyzed back to the free parent drug. Un-degraded molecules are then discharged to receiving surface waters or find their way to groundwaters (e.g., via leaching or purposeful recharge). Extensive overviews of the topic have been presented in review articles [1, 3-7], in an upcoming ACS book [8], and on a U.S. EPA website devoted to the topic [9].

Mass spectrometry provided the underlying capability for the scientists who have elucidated this "emerging" topic largely over the course of the last 10 years. As such, this is just one of countless examples of how mass spectrometry has played a leading (albeit largely invisible) role in the communication of major environmental knowledge and lessons to the public over the last 30 years. Its continuing future role for yet other currently unrecognized chemical risks will surely continue.

As an historical aside, probably the first report of a prescription drug in the environment (sewage treatment effluent) was made over 20 years ago (see summary in [1]) and was that of clofibric acid, the active metabolite from the high-volume, high-dosage lipid regulators clofibrate, etofibrate, and theofibrate. While this data was acquired over 20 years ago (and was pointing to the possibility that the continual, daily introduction of substantial quantities of drugs and bioactive metabolites from the combined excreta of end-

users to and from sewage treatment plants into receiving waters could result in sustained environmental concentrations of PPCPs), the larger phenomenon was not really recognized until the 1990s, with the advent of in-depth studies targeted for PPCPs. Clofibric acid is one of the more persistent PPCPs; and it reaches concentrations (e.g., sub-ppb) in open waters on par with those of many "conventional" pollutants, such as the POPs ("persistent organic pollutants"). Clofibric acid presents an interesting historical aside. As a phenoxyalkanoic acid, the achiral clofibric acid (2-[4-chlorophenoxy]-2-methylpropionic acid) is a structural isomer of the enantiomeric herbicide "mecoprop" (2-[4-chloro-2-methylphenoxy]-propanoic acid). Both of these compounds can co-occur in waters. While the methyl esters of both compounds can be separated by gas chromatography, their EI mass spectra both share molecular ions of *m/z* 228 as well as a major fragment at *m/z* 169. Other than these two ions, however, the use of EI mass fragmentation (Fig. 3) affords distinctive patterns (largely because of the chlorophenol moiety) that can be compared with those of standards. Mass spectrometry has played a key, but behind-the-scenes, role in sorting out environmental forensics problems such as this one for many years.

Critical Role of Environmental Chemistry: The National Research Council (as requested by the National Science Foundation) synthesized the broad expertise from across the many disciplines embodied in environmental science to offer its judgment as to the *most significant environmental research challenges of the next generation* – based on their "potential to provide a scientific breakthrough of practical importance to humankind if given major new funding".

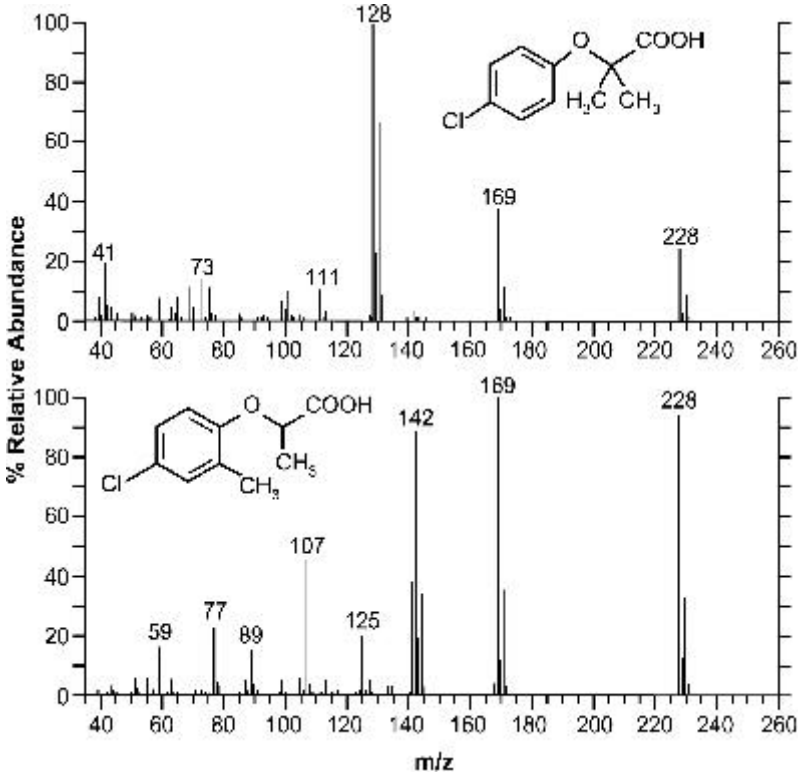

Figure 2. EI mass spectra of the methyl esters of two ubiquitous and persistent bioactive phenoxyalkanoic acid pollutants. Both are structural isomers (structures of the free acids are displayed): the antilipidemic drug metabolite clofibric acid (upper spectrum; 2-[4-chlorophenoxy]-2-methylpropionic acid) and the herbicide mecoprop (lower spectrum; 2-[4-chloro-2-methylphenoxy]-propanoic acid). [spectra adapted from H.-R. Buser et al. *Environ. Sci. Technol.* **1998**, *32*(1), 188-192]

Of the eight "grand challenges" identified in the NRC's report (*Grand Challenges in Environmental Sciences* [10]), two require concerted input from those involved with pollutant identification: (1) "Hydrologic Forecasting" (for predicting changes in freshwater resources as a result, in part, of chemical contamination – a concern, for example, regarding PPCPs) and (2) "Reinventing the Use of Materials". The impetus driving the second is

> "...new compounds and other substances are constantly being incorporated into modern technology and hence into the environment, with insufficient thought being given to the implications of these actions. All of these issues assume added importance in urban areas, which concentrate flows of resources, generation of residues, and environmental impacts within spatially constrained areas. From a policy standpoint, reliable predictive models of material cycles could be invaluable in guiding decisions about ... topics relating to human-environment interactions..." "This grand challenge centrally encompasses questions about societal-level consumption patterns, since consumption is the primary force driving human perturbations of material cycles."

"Emerging" Chemical Risks: One of the "signature science" responsibilities of the U.S. EPA's Office of Research and Development (ORD) (as well as for other environmental science institutions throughout the world) is to pioneer and nurture new programs for identifying, evaluating, and developing the requisite science for minimizing existing – or preventing future – exposure risks from previously unrecognized and unexpected chemicals. By using various approaches to discovery, "futuring" (e.g., see: http://www.geocities.com/CapitolHill/Senate/4787/index.html/ and http://www.epa.gov/ordinter/futures/), and fast failure analysis, a major objective is to minimize the time required to transfer new science to other parts of the Agency, to other government agencies and research institutions, and to the public. This type of science can eventually guide society away from a reactionary mode of being forced to deal with entrenched environmental problems, and instead orient it more towards proactive, preventative science.

The term "emerging" only reflects one aspect of the overall issue surrounding the need to minimize or prevent exposure risks. Because of this, the term "emerging" can misrepresent and obscure the overall issue. Those risks emanating from chemical pollution can be classified into four main categories: (1) Growing/Developing, (2) Hidden/Latent, (3) Emerging, and (4) Future. Clearly, the term "emerging" only accounts for one of four possible categories of previously unrecognized or unanticipated exposure risks – but this term is nonetheless used to encompass all four categories. The following presents a discussion of these four areas of concern with respect to chemical pollution and how to view them under one umbrella.

Importance of Chemical Exposure in Health: As the more important determinant of overall health (i.e., as measured at least by certain cancers), the *exposure environment* rather than *genetics* is becoming more firmly established (e.g., note one of the most thorough studies to date using birth twins [11]).

While genetics obviously sets the stage (genotype) for health, the chemical environment to which an organism is exposed defines and molds the actual character (phenotype) in which an organism actually manifests itself. The chemical sea in which an organism develops, matures, and subsists comprises substances essential to life (nutrients) as well as those adverse to life – both naturally occurring xenobiotics and anthropogenic pollutants. The latter includes substances purposefully designed and synthesized (sometimes with the intent to adversely affect organisms, e.g., pesticides, antimicrobials) and those that are inadvertent (and sometimes hidden) by-products of manufacture, consumption, metabolism, and environmental transformation. This partial accounting of the potential chemical-exposure universe is immense, possibly comprising millions of substances.

Those substances subject to EPA's historical regulatory framework possibly represent but a small subset – largely a result of expediency and necessity. The majority of the quantities and individual chemicals released to the environment by permitted dischargers are not regulated; few chemicals released to the environment by consumers are regulated. Just because these "uncontrolled" pollutants are not classified as "priority" pollutants does not mean that they do not pose risks. This is the major impetus behind the emergence (primarily in Europe) of the Precautionary Principle [12].

Need for Holistic Exposure Assessments: The exposure environment to which environmental toxicologists have traditionally focused their attention is limited to the "conventional" pollutants that comprise the various lists of regulated pollutants (also called "criteria", "priority", or "legacy" pollutants). These are primarily the "high-volume" industrial chemicals (and manufacturing by-products), nutrients, and those substances specifically designed to kill pests. It is important to note that the feature distinguishing these several hundred chemicals is the fact that they are produced and consumed in the highest quantities amongst all chemicals. Unfortunately, these chemicals comprise but a very small portion of the universe of xenobiotics to which organisms can and do suffer exposure. While the numbers of regulated pollutants *worldwide* total about 220,000 (as of 2001; see: http://www.cas.org/CASFILES/chemlist.html/), only a small portion of these are routinely monitored for occupational or environmental purposes. In stark contrast, the numbers of synthetic and naturally occurring xenobiotics constituting the potential exposure universe probably comprise many hundreds of thousands; this is undoubtedly a conservative estimate given that Chemical Abstracts Service has registered over 15 million organic and inorganic substances (as of 2001), and over 1,800,000 of these are readily commercially available (http://www.cas.org/cgi-bin/regreport.pl/). When considering the high-profile, regulated categories of chemicals, regulators have not been able to consider the complexities and ramifications of complete exposure profiles, including the full range of bioactivity of all parent substances (and the multitudes of transformation products), or their exposure frequency, exposure duration (sustained cumulative effects), or exposure complexity (aggregate or cumulative exposure or synergism). Given this limitation, it is critical that holistic assessments of the wide range of potential environmental pollutants be made and to pinpoint those pollutants with highest health-effects potential.

To this end, an objective of EPA ORD science is to (i) elucidate a more rounded, expanded view of the exposure universe, (ii) at least be better prepared to cope with newly identified or previously unrecognized pollutants, and (iii) lay the foundation for developing an ultimate ability to foresee/predict potential chemical pollution problems before they develop. As such, this work relates to the unknown rather than to the better-defined exposure world that we have come to greatly understand over the last 40 years.

"Emerging" Issues and Short-Circuiting Risk: The type of work described here is often referred to as "emerging issues". The term "emerging," however, is highly overused -- one whose banner is frequently raised in many fields of study – from politics and economics to math, ecology, and epidemiology. In particular, "emerging" has a long-established, strong connotation associated with pathogens and infectious diseases (e.g., at the U.S. Food and Drug Administration [FDA] and the Centers for Disease Control and Prevention [CDC]). In addition, for reasons discussed below, "emerging" is not the best descriptor for the work required with PPCPs or most other previously unrecognized pollutants. "Emerging" is a misnomer with respect to chemical pollution because many or most of the instances in which it is employed deal either (1) with issues that have existed for some time and have eluded our attention for a variety of reasons, or (2) those issues that have yet to occur. Only a fraction of cases involve new problems that are truly just in the process of occurring or developing -- *emerging*.

The Varied Dimensions of the Exposure Continuum: Previously unrecognized, unexpected, or unanticipated scenarios of exposure to chemicals can be pursued or viewed from a number of different

perspectives. There are several different dimensions that can account for the universe of potential chemical toxicants. From each of these dimensions comes a different perspective in terms of how the chemical universe "pie" or continuum is sliced. These different perspectives often inject confusion into discussions oriented to anticipating future risks or uncovering existing, but previously unrecognized, risks. Further complicating the multidimensioned view of chemical exposure risks is the fact that the various subsets of chemicals comprising each of these different perspectives can overlap to various degrees -- portions of each subset can belong to others.

Previously unrecognized chemical exposure risks can be delineated based on the following "dimensions":

- **chemical classes** (according to chemical functionality: chemicals of totally new structure)
- **type of use** (new uses in either the industrial or consumer realms)
- **type of effect** (newly discovered but prior-existing effects or totally new receptor targets or ligand-receptor interactions)
- **source** (new or previously unknown origins for existing chemicals)
- **exposure** (pathways that had not been anticipated -- or previously discounted as not possible)

The following (now historical) examples using PPCPs are provided for each of these "dimensions" to clarify the distinctions among them:

- New chemical classes: angiogenesis inhibitors
- Type of use: sexual dysfunction (e.g., Viagra); selective serotonin reuptake inhibitors (SSRIs)
- Type of effect: "endocrine disruptors"; broad-spectrum efflux pump inhibitors; NO regulators (e.g., Viagra); COX-2 inhibitors
- Source/matrix: humanitarian assistance projects as a source of drugs in environment from disposal; drinking water as source of unintentional multi-drug ingestion; drugs used for pest control†
- Exposure route: ingestion of synthetic musk fragrances via fish; inhalation of drinking water disinfection by-products via showering

†Many drugs have not just multiple therapeutic uses but sometimes uses unrelated to therapy. Examples include: < 4-aminopyridine: experimental multiple sclerosis drug and an avicide; < warfarin: anticoagulant and a rat poison; < triclosan: general biocide and gingivitis agent used in toothpaste; < azacholesterols: antilipidemic drugs and avian/rodent reproductive inhibitors [e.g., Ornitrol]; < certain antibiotics: used for orchard pathogens; <acetaminophen: an analgesic and useful for control of brown tree snakes.

Even though these distinctions of perspective make no difference with respect to the technical design, implementation, or understanding of research in this area, they can have a dramatic impact in the communication of the work to non-experts. As an example, the issue of endocrine disruption slices the pie along the "effects" axis, while at the same time cuts across several other axes -- for example, endocrine disrupting compounds (EDCs) comprise substances from numerous chemical classes, and they can have many different commercial and consumer end uses. Among EDCs are certain drugs (which represent a broad "use" class) -- but only a certain small percentage of drugs are "direct-acting" EDCs (i.e., hormone receptor agonists/antagonists). Alternatively, if one slices the universe of chemicals along the type-of-use axis, all pharmaceuticals can be embraced in a broad category -- and while some of these are EDCs, the remainder have a multitude of effects removed from that of the immediate endocrine system. Each axis

can yield a slice of the chemical universe, which in turn provides a unique view of the exposure continuum.

Terms to Categorize the Continuum of Risk: There is actually a continuum of terms, each of which partly categorizes a portion of the work that needs to be done with respect to addressing the world of what we inaccurately refer to as "emerging issues" or "emerging science" -- specifically, "emerging pollutants". This continuum comprises:

(0) **Long-Established, Widely Recognized Risks**: these constitute the vast majority of the U.S. EPA's historic business regarding chemical pollution, such as POPs, "persistent bioaccumulative toxicants (PBTs), and nutrients.

(1) **Unexpectedly Growing/Developing Risks**: pre-existing, but already recognized low-level potential that has now unexpectedly grown to become a newly recognized risk (data were available to recognize the potential for on-set of a risk but the heightened risk developed unexpectedly).

(2) **Hidden, Latent Risks**: those previously unrecognized risks that have already existed for some time but are just becoming recognized, uncovered, or discovered (this category includes chemicals not known to already exist in the environment as well as existing, "unassessed" chemicals of historically little concern but which harbor unexpected/unpredicted effects) [success controlling these risks results via remediation and pollution prevention].

(3) **Emerging, Nascent Risks**: those that have not previously existed and which are just beginning to develop or "emerge" (this category involves new chemicals never before existing as well as from new uses for old chemicals; there is a need to pay more attention to those chemicals whose uses have little or no regulation) [success controlling these risks results in "early warning"].

(4) **Future Risks, Currently Non-Existent Risks**: those that do not currently exist but which can be foreseen, predicted, or anticipated [success here results in outright prevention of risk that *could*/*would* have otherwise occurred].

If we pause to consider PPCPs in this framework (as illustrative cases), it is clear that with the exception of new-generation PPCPs (not previously existing), these chemicals all fall within category 2 (previously unrecognized risks) because they have undoubtedly had the potential to occur in the environment ever since they became commercially available (in many cases decades ago) and within category 1, since their prevalence in the environment is increasing as a result of increasing consumption, expanding therapeutic targets, and increasing population, among other reasons. New-generation drugs subject to the FDA approval process would usually fall under category 4.

For the last 20-30 years, EPA's research has generally focused on long-established risks (involving the "conventional," regulated "legacy" pollutants, many of which, such as the POPs, have presented intractable, refractory problems – Category 0). Together with categories 1 and 2, these are the three main areas of chemical pollution on which environmental protection/regulatory bodies have traditionally focused -- and out of necessity almost exclusively in a *reactive* mode. All of the other chemicals that comprise categories 1 and 2 can be referred to as unassessed or un(der)addressed chemicals or non-regulated/non-conventional pollutants.

Category 3 (emerging risks) occur only when newly introduced chemicals or by-products enter (or are created within) the environment, or when new, uncontrolled sources come on line. Perchlorate was somewhat in this category as well as category 2. Many little-discussed chemicals belong to category 2

simply because of years of neglect; a case in point being the numerous members of dust/erosion-control agents, substances that can be used in very large quantities.

Clearly, society's major desire would be to focus and succeed with Category 4 so that resources that would otherwise have to be devoted to Categories 1-3 can be minimized or eliminated. This would allow society to get and remain ahead of the curve – to be proactive rather than reactive – to focus on pollution prevention rather than remediation. Progress in Category 3 provides early warning, which also helps to minimize resources that would need to be devoted to an otherwise larger problem. Instead of focusing on identifying "emerging"concerns (Category 3) – which is still a reactive way of protecting health – it would be better to cast our efforts proactively, to minimize future risk and correct "yet-to-be-identified risks" – to "combat future, would-be risks". But this cannot be done until the existing risks have been fully elucidated. Mass spectrometry will undoubtedly continue to play a key role in this endeavor for years to come.

Two High-Priority Needs in Environmental Analytical Chemistry: Two long-standing needs for enhancing our sentinel ability to corral emerging contaminant issues are: (i) enrichment techniques for preconcentrating from aqueous media not just hydrophobic compounds, but also polar substances, and (ii) automated approaches to mass spectrometry for *non-target* analysis. Respective examples include: (i) devices [13,14] designed to collect polar compounds from large volumes of water, and (ii) a high-resolution mass spectrometry approach [15] for rapidly narrowing the universe of molecular compositions for non-target unknowns. These needs are particularly important for extending our knowledge of PPCPs in the environment.

...And Many Others: Additional avenues await advancements from newer or better applications of mass spectrometry. Chirality is one. The bioactivity of drugs is (not surprisingly) often controlled by their optically active forms. Chirality plays a very large role in the biochemistry of drugs. While nearly all drugs derived from natural sources are expectedly homochiral, synthetic single-enantiomer drugs (or those with specifically designed enantiomeric ratios) are only beginning to be used (see Table I). Biodegradation discriminates among isomers leading to tell-tale enrichment of one form over another. This can potentially alter the toxicity of the residues (chiral drug isomers can work in synergy or against each other [e.g., one can give adverse effects], or one can be inactive) as well as be used to "fingerprint" the weathered status of residues. Traditionally, mass spectrometry has been believed to not be useful to differentiate chirality. But its potential for fast chiral discrimination and detection of low enantiomeric excesses would be useful for a variety of purposes (including the verification and tracking of the "performance" of natural attenuation for site cleanup). Another need is for identification of protein sequencing (peptide mapping) in the proteomics, a field that holds tremendous importance for both drug discovery (via identification of new targets) and prediction of health effects from environmental exposure. Mass spectrometry has already played a large role in elucidating ligand binding but continued advances are needed.

Table I. Synthesis-Origin and Chiral Distribution of Discrete Drugs Worldwide[1]

		Chiral		
source	Achiral	Racemic	Single Enantiomer	*worldwide totals*
natural (or derived analog)	6	8	509	523
synthetic	799	467	61	1327
worldwide totals	805	475	570	1850

[1]adapted from: W. Locke, *The Alchemist*, January 2001: http://www.chemweb.com/alchem/articles/985883680391.html

Expanding Your Horizons – Seizing New Perspectives: Now, returning to "why elevator rides can be important for your career and for your discipline," some closing words on communicating our science.

• **The "Elevator Speech":** Can you explain to your captive elevator audience (when ascending from the first to fourth floors) not just what you *do* and what it *involves*, but WHY it's important to them? Force yourself to initiate discussions with people who may have no clue as to what your work is about – see if the glassy-eyed stares end your monolog prematurely. Long-known in the corporate community as the "elevator speech", it can be one of the most important presentations you ever deliver. It can open doors for future opportunities, and it can expand the horizons of all. So the next time someone asks "...and what do you do?" -- resist the reflexive "I'm a mass spectrometrist" or some such, and instead say something to the effect "My laboratory research at -...- improves the -...- of citizens by developing new aspects of chemistry that are important to you because -...-" This is your "sound bite" for the listener to subconsciously memorize -- hopefully for later recitation to others. End your "speech" by asking what the single most important thing you could do in the future as a scientist to help them further understand the importance of science. For imparting more perspective, tell your listeners what would happen if you were NOT engaged in the work you do -- e.g., what would happen if mass spectrometry ceased to be practiced? Remember that your communication is not just for your sake, but also for the continued advancement of your field. To successfully communicate with those in other professions, one must learn to cast ideas in the frame of understanding used by others. As an example, the need is rapidly growing for environmental scientists to communicate with the mainstream business community so that environmental objectives and policies that are both scientifically and economically sound can be embraced, valued, and championed by BOTH business and science.

• **The doors can open onto floors you never knew existed:** Make a habit of reading well outside your area of expertise or interest – in both the technical and the lay literatures. New, totally

unforeseen perspectives can be gained rapidly. At conferences, attend some sessions outside your specialty or established interests. You might find that the perspectives of others can help you expand your horizons. Reciprocally, your expertise might be of critical use to them. The lay person can unexpectedly provide perspectives on your work that you never contemplated (or reinvigorate your own interests), thereby opening new avenues of research. Conference organizers can gain tremendous perspective by having journalists give concluding remarks -- to relate what *they* heard at the meeting -- which may surprise the participants and attendees and give them a better appreciation for how difficult effective communication can be.

• **Capitalize on the Unexpected**: Although measurement of performance is designed to target intended or anticipated outcomes, sometimes unanticipated outcomes can have significant importance. By way of example, for the issue of PPCPs in the environment, perhaps the major unanticipated outcome to date has been the value of the topic in imparting knowledge of environmental science to the lay public (including schools, public, and the media). The public makes a natural connection to the topic -- because it demonstrates first hand the interconnectedness of humans and their environment – a connection that is immediate, intimate, and inseparable.

• **Marketing versus Selling**: Simply explaining what we do as researchers (selling our wares) is but one dimension of successful science. More important is identifying those societal needs to which our work can contribute and "make a difference". The extension or development of new knowledge is only one aspect of our work – we must be able to explain what it means, and put it to use. This is the all-important "value-added" aspect of our work. In Bruce Alberts' 2000 President's Address to the National Academy of Sciences ("Science and Human Needs", available at: http://www.nas.edu), he addresses in part "the responsibilities of scientists" with the following words:

> "... (B)ecause political will is often short term, and misinformation about science abounds, we scientists ourselves must become much more engaged in the everyday life of our governments and our communities." As 'civic scientists', "...in the 21st century, science and scientists will be judged on how well they help solve local and world problems, not only on how well they generate new knowledge. The impact of our research is everywhere, and we must step out and make sure that our work is understood and appropriately used by the world. ...We also need to be explicit about what is not known, and be clear about the questions that science cannot answer."

In Donald Stokes' "Pasteur's Quadrant" [16], a model is constructed where strictly *knowledge*-oriented research (called the "Bohr quadrant") lies diametrically to strictly *use*-oriented research (the "Edison quadrant"). With increasing pressure over the last decade to shift funded research away from the Bohr quadrant (knowledge for knowledge's sake), in order to gain funding, newly proposed research is often forced into the Edison quadrant. Many believe this breeds a dangerous vulnerability for eroding science's foundation upon which future advancements can be built. A fused balance of the two quadrants resides in the "Pasteur quadrant", where a constant communication between all stakeholders (and potentially interested parties) can ensure that the pursued work will result in contributing to construction of road maps that lead to destinations of value while at the same time giving the future ability to sail into currently uncontemplated, unchartered waters.

• **Spend time at the edges (remember, interesting chemistry happens at interfaces):** Just as many interesting environmental processes (not the least of which was perhaps the beginnings of life)

occur at complex media interfaces, the same applies to disciplines. The perceived value of disciplines onto themselves – studies in isolation – is diminishing as the interconnected complexities of nature and society become more evident to the scientist and public alike. The birth of new knowledge, insights, and ideas is clearly catalyzed in the cauldron-like interfaces where multiple disciplines can coalesce. This method for unleashing creativity was adopted by Hewlett-Packard Co. in 2000 for their vast restructuring, and was referred to as "inventing at the intersection" by CEO Carleton Fiorina. Try to communicate – or better yet, collaborate – with scientists in other disciplines. If you don't think that any linkage is possible between mass spectrometry and social science, business, or entertainment engineering, try to find out in person. Work outside your comfort zone, expand your envelope, and embrace what was once not there.

- **The Fragmentation of Science - Loss of the Bigger Picture (Critical Importance of Knowledge "Mining" and Synthesis):** Where and how does your work fit into the larger scheme? Much of the world's published science literature is vastly underutilized and highly fragmented. With respect to environmental aspects of PPCPs, for example, the medical literature in particular has yet to be effectively utilized to address ecological effects questions. While the information available in any research field continues to grow exponentially, proportionately less time is devoted in trying to "mine" and capture this knowledge to synthesize a larger picture.[‡] Literature is often ignored or simply becomes "lost" to future investigators. The paradoxical message is that the published literature is not as important as "new" findings. Duplication of effort and reinvention of the wheel are symptoms of the failure to pay sufficient attention to the literature. A parallel problem is that the larger picture remains obscure when the literature is not critically examined, especially for issues that cross multiple disciplines. Solutions to problems and answers to questions can be waiting to be "discovered" amidst research that has already been reported. But the literature is also corrupted with misinformation and inaccuracies, all of which must be filtered out. *True brilliance resides in the ability to filter the errant from the cogent.*

> [‡][Note that "mining" is used here in the sense of "knowledge" not "data". The latter pertains to the tool called meta-analysis – not to general knowledge as a synthesis of ideas, concepts, insights, perspectives, etc.]

This problem results in part from the fact that there is little professional reward in attempting to distill, synthesize, and integrate what is known about a topic. Science managers tend to value publication of "original" data -- even if it is incremental, and even, unbeknownst them, if it is merely "rediscovered" data. Furthermore, scientists often have little time to understand the significance, impact, or relevance of their work because they are caught in the drive to publish -- at the expense of reading, comprehending, distilling, synthesizing, and communicating the relevance of their work.

The issue of "capture and synthesis" of fragmented knowledge has been cogently discussed [17] by Prof. Peter Csermely (Semmelweis University, Budapest). Csermely argues that little attention is being paid to the fragmentation of the world's science literature. This is a major reason that it is so extremely difficult for individual scientists to have a broad-based appreciation for the "bigger picture". Csermely writes: "There is only a limited effort to achieve the appropriate balance between the discovery of new facts and finding their proper place and importance in the framework of science." This relates partly to what can be referred to as understanding the "significance", "impact", or "relevance" of one's work. Csermely goes on to note that "science itself is not self-integrating, and there are fewer and fewer people taking responsibility for net-making". "Integration [of knowledge] needs time and patience..." "...greater credit should be given to those who make serious attempts to integrate their findings into the whole of human knowledge."

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